with an antibody directed against the epitope-tag[,];

d) isolating the antibody-bound yeast protein(s) obtained in c) and purifying them[,];

e) determining the sequence of the yeast protein(s) obtained in d)[,]; and

f) identifying the human subunit(s) by comparing the sequence(s) of the yeast protein(s) obtained in e) and/or the DNA sequence encoding [those] said yeast proteins with published human sequences.

A1 Cont'd.

2. (Amended) The method of claim 1, wherein the gene(s) used in [step] a) are selected from the group consisting of *APC1*, *CDC16*, *CDC23*, *CDC26*, *CDC27*, *APC2*, *APC5*, *APC4*, *APC9* [*and*] and *APC11*.

3. (Amended) A method for identifying novel subunits of the human Anaphase Promoting Complex (APC), [characterized by the steps] comprising:

a) replacing in a human cell one or more endogenous genes encoding known APC subunits by epitope-tagged versions of said genes or transforming the cell with a vector containing the corresponding epitope-tagged cDNA(s) and establishing a cell line[,];

b) growing the cell line obtained in a) and preparing a protein extract[,];

c) isolating the APC by contacting the protein extract obtained in b) with an antibody directed against the epitope-tag[,];

d) isolating the antibody-bound protein(s) obtained in c) and purifying them[,]; and

e) determining the sequence of the protein(s) obtained in d).

A1 Cont'd.

4. (Amended) The method of claim 3, wherein the gene(s) or the respective cDNAs used in [step] a) are selected from [a] the group consisting of genes that are homologs of the yeast genes *APC1*, *CDC16*, *CDC23*, *CDC26*, *CDC27*, *APC2*, *APC5*, *APC4*, *APC9* [*and*] and *APC11*.

5. (Amended) A method for producing recombinant APC, [characterized in that] comprising expressing cDNAs encoding APC subunits [are expressed] in a suitable host, isolating and purifying said subunits [are isolated, purified] and [allowed] allowing said subunits to assemble to form a functional APC.

Please cancel claims 7-10 and insert the following new claims:

11. A method for identifying substances that inhibit rapidly proliferating cells by interfering with the cells' entry into the subsequent cell cycle, comprising reacting recombinant APC with a test substance, a ubiquitin activating enzyme, a ubiquitin conjugating enzyme, an epitope-tagged ubiquitin, ATP and a substrate, and measuring the resulting amount of immobilized ubiquitin to determine the effect of the test substance on the APC's ability to ubiquitinate the substrate.

A2 Cont'd.

A2 concld.

12. The method of claim 11, wherein the APC and the substrate are of human origin.

13. The method of claim 11, wherein the substrate is a recombinant cyclinB.

Remarks

Upon entry of the foregoing amendment, claims 1-6 and 11-13 are pending in the application, with claims 1, 3, 5 and 11 being the independent claims. Claims 7-10 are sought to be canceled without prejudice to or disclaimer of the subject matter therein. New claims 11-13 are sought to be added. Claims 1-5 were amended to conform with U.S. practice. Support for new claims 11-13 is found throughout the specification, *e.g.*, in original claims 7-10 and in the specification, pages 7-8. These changes are believed to introduce no new matter.

It is believed that the application is now in condition for examination. Early notice to this effect is respectfully requested.

Respectfully submitted,

STERNE, KESSLER, GOLDSTEIN & FOX P.L.L.C.

Raz E. Fleshner
Attorney for Applicants
Registration No. 34,331

Date: July 14, 1999

1100 New York Avenue, N.W., Suite 600
Washington, D.C. 20005-3934
(202) 371-2600

P:\USERS\kvidovic\0652\1880000\P91-95.wpd